

AN 1993:24009176 BIOTECHNO  
TI Actions of interleukin-4 on prostaglandin biosynthesis at the  
chorion-decidual interface  
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SO American Journal of Obstetrics and Gynecology, (1993), 169/6 (1442-1447)  
CODEN: AJOGAH ISSN: 0002-9378  
DT Journal; Article  
CY United States  
LA English  
SL English  
AB Objective: We determined the effects of interleukin-4 on chorion and decidual prostaglandin production. Study design: Chorion and decidual cells from term placentas were grown to confluence. Cells were then incubated with interleukin-4 either alone or with other known stimulants of prostaglandin production: interleukin-1 $\beta$ , epidermal growth factor, ionomycin, or phorbol 12-myristate 13-acetate. Prostaglandin E.sub.2 production was determined with a specific radioimmunoassay.  
Results: Interleukin-4 alone stimulated prostaglandin E.sub.2 production in chorion and decidual cells. Interleukin-4 significantly enhanced the stimulatory actions of phorbol 12-myristate 13-acetate, ionomycin, and epidermal growth factor but not interleukin-1 $\beta$  on prostaglandin E.sub.2 production. Conclusion: Interleukin-4 stimulates prostaglandin E.sub.2 production by chorion and decidual cells. These data suggest that interleukin-4 production by immune effector cells in gestational tissues may contribute to the pathophysiologic features of preterm labor  
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CT. . . growth factor; interleukin 1beta; ionomycin; phorbol 13 acetate 12 myristate; article; cell culture; controlled study; human; human cell; placenta; premature labor; priority journal; radioimmunoassay; etiology  
RN (prostaglandin e2) 363-24-6; (epidermal growth factor) 62229-50-9;  
(ionomycin) 56092-81-0; (phorbol 13 acetate 12 myristate)  
16561-29-8

AN 1998:226095 BIOSIS  
DN PREV199800226095  
TI Involvement of phosphatidate phosphohydrolase in arachidonic acid mobilization in human amnionic WISH cells.  
AU Balboa, Maria A.; Balsinde, Jesus; Dennis, Edward A. [Reprint author]  
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SO Journal of Biological Chemistry, (March 27, 1998) Vol. 273, No. 13, pp.  
7684-7690. print.  
CODEN: JBCHA3. ISSN: 0021-9258.  
DT Article  
LA English  
ED Entered STN: 20 May 1998  
Last Updated on STN: 20 May 1998  
AB Prostaglandins are known to play a central role in the initiation of labor in humans, and amnionic cells constitute a major source of these compounds. Prostaglandin synthesis and release by amnion cells in response to hormones and ligands takes place after a characteristic 4-5 h lag. However, we report herein that free arachidonic acid (AA), the metabolic precursor of prostaglandins, can be induced at much shorter times (1 h) in human amnionic WISH cells by phorbol 12-myristate 13-acetate (PMA) through activation of protein kinase C $\alpha$  (PKC $\alpha$ ). WISH cells were found to possess both cytosolic group IV phospholipase A2 (cPLA2) and Group VI Ca $^{2+}$ -independent phospholipase A. (iPLA2). Of these, the cPLA2 was found to be the likely mediator of AA mobilization in PMA-activated WISH cells. PMA also activates phospholipase D (PLD) in these cells and ethanol, a compound that inhibits PLD-mediated phosphatidic acid (PA) formation, blocked AA release. Moreover, prevention of PA dephosphorylation by the PA phosphohydrolase inhibitors propranolol and bromoenol lactone, resulted in inhibition of AA release by PMA-treated-WISH cells. Collectively, these data suggest that activation of cPLA2 and attendant AA release by phorbol esters in WISH cells requires prior generation of DAG by phosphatidate phosphohydrolase.  
AB Prostaglandins are known to play a central role in the initiation of labor in humans, and amnionic cells constitute a major source of these compounds. Prostaglandin synthesis and release by amnion cells in.  
RN 506-32-1 (arachidonic acid)  
16561-29-8 (phorbol 12-myristate 13-acetate)  
9025-77-8 (phosphatidate phosphohydrolase)  
9001-84-7 (phospholipase A)  
9001-87-0 (phospholipase D)  
141436-78-4 (PROTEIN KINASE C)

DOCUMENT NUMBER:  
127:146000

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127:146000

TITLE:  
An analysis of the mechanisms involved in the  
okadaic acid-induced contraction of  
the estrogen-primed rat uterus

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CODEN: JFETAB; ISSN: 0022-3565

PUBLISHER: Williams & Wilkins

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LANGUAGE: English

AB The contractile effect of **okadaic acid** (OA) and its (20  $\mu$ M) induced a transient contraction which, after plateauing, slowly decreased. The structurally related compound Okadanol (20  $\mu$ M) failed to induce any significant contraction. Conversely, the synthetic compound Me okadaate (20  $\mu$ M) and the naturally occurring ester 7'-hydroxy-4'-methyl-2'-methylenehept-4'-(E)-enyl okadaate (20  $\mu$ M) were as active as the free acid. The OA-induced contraction was unaffected in the presence of neomycin (5 mM), mepacrine (30  $\mu$ M), 1-[N,O-bis(1,5-isoquinolinesulfonyl)-N-methyl-L-tyrosyl]-4-phenylpiperazine (10  $\mu$ M), calphostin C (3  $\mu$ M) and 1-(5-isouquinololinylsulfonyl)-2-methylpiperazine (30  $\mu$ M). The calmodulin inhibitor N-(6-aminohexy1)-5-chloro-1-naphthalenesulfonamide hydrochloride (100  $\mu$ M) did not modify the amplitude of the OA-induced contraction but significantly increased the rate of tension decay. The myosin light chain kinase inhibitor 1-(5-chloronaphthalene-1-sulfonyl)-1H-hexahydro-1,4-diazepine hydrochloride (1 mM) significantly reduced the peak amplitude of the contraction. Staurosporine (0.03-0.1  $\mu$ M) did not inhibit the contractile component of the OA-induced response but inhibited the subsequent decrease in tension. In freshly dispersed myometrial cells loaded with the fluorescent  $\text{Ca}^{++}$  indicator indo-1, OA did not produce any significant increase in  $[\text{Ca}^{++}]_i$ . OA (5- to 90-min contact) also failed to modify the intracellular levels of arachidonic acid, compared with basal values. These data suggest that in the rat uterus (1) the contractile effect of OA (20  $\mu$ M) is specifically mediated by inhibition of protein phosphatases type 1 and/or 2A and is related to a direct interaction with the contractile machinery; (2) the decreasing phase of the OA-induced mech. response could be mediated by a staurosporine-sensitive protein kinase C.

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MEK inhibitor U0126 delays RU486-induced preterm labor  
in rats.

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CS Harvard-Med.Sch.; Univ.Boston

LO Boston; Watertown, Mass., USA

SO Anesthesiology (98, Suppl. 1, 11, 2003) 4 Ref.

CODEN: ANESAV ISSN: 0003-3022

AV Beth Israel Deaconess Medical Center, Harvard Medical School, Boston,  
Massachusetts, U.S.A.

LA English

DT Journal

RA AB; LA; CT

FS Literature

AN 2003-24475 DRUGU P

AB The effect of the MEK activation inhibitor U-0126 on RU-486-induced pre-term labor was investigated in Sprague-Dawley rats. 18-Day pregnant rats were pretreated with U-0126 (100 mg/kg/6 hr, s.c.) and labor was induced on day 19 with RU-486 (2 mg/kg, s.c.). Treatment with U-0126 delayed the onset of parturition to an average of

25.18 hr after RU-486. Delayed labor was associated with activation of ERK2 and phosphorylation of caldesmon in myometrium compared to the sham group. Results suggest that the ERK/caldesmon pathway might be used a target for the development of tocolytics. (conference abstract: Society for Obstetric Anesthesia and Perinatology 35th Annual Meeting, Phoenix, Arizona, USA, May 14-17, 2003). (No EX).

ABEX (E97)

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CT [01] U-0126 \*PH; LABOR \*OC; DR9800013 \*RN; IN-VIVO \*FT; RAT \*FT;  
S.C. \*FT; TOCOLYTIC \*FT; CALDESMON \*FT; EC-2.7.1.37 \*FT; LAB.ANIMAL  
\*FT; INJECTION \*FT; PROTEIN-KINASE.